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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Hans Rudolf MÜLLER et al.

Confirmation No.: 8617

Serial No.: 10/030,693

Examiner: Tamthom Ngo Truong

Filed: January 14, 2002

Group Art Unit: 1624

Title: PROCESS FOR THE PREPARATION OF PURE STEREOISOMERS OF
TETRAHYDROFOLIC ACID ESTER SALTS AND TETRAHYDROFOLIC
ACID BY FRACTIONATED CRYSTALLISATION OF TETRAHYDROFOLIC
ACID ESTER SALTS

REPLY AFTER FINAL REJECTION

MAIL STOP AF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the final Office Action mailed December 29, 2003, kindly amend the
above-identified application as follows.

Amendments to the **Specification** begins on page 2 of this paper.

Amendments and additions to the **Claims** are reflected in the listing of claims which begins
on page 5 of this paper.

Remarks/Arguments begin on page 11 of this paper.

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Art Unit: 1624

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Claim 18: on line 4, delete the phrase "**tetrahydrofolic acid or**".

(see attachment)

Authorization for this examiner's amendment was given in a telephone interview with Mr. James E. Ruland on 05-24-04.

Allowable Subject Matter

Applicant's amendment of 04-28-04 has been fully considered. The amended claims and specification have overcome the previous rejections of 112/2nd paragraph and 102(b) based on the teaching of **Müller et. al.** (US'836). With claims 3-5, 8, 9, 13, 15 cancelled, pending claims 1, 2, 6, 7, 10-12, 14, 16-23 are allowed.

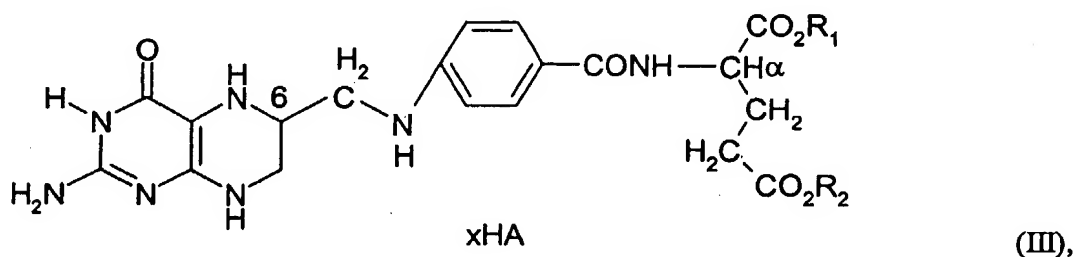
Reason for Allowance

The following is an examiner's statement of reasons for allowance:

The invention is drawn to a process of preparing and concentrating (6S, α S) or (6S, α R) tetrahydrofolic acid or

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18. (Currently Amended) A process for preparing and concentrating a (6S,αS) or (6S,αR) tetrahydrofolic acid ester salt or a (6S,αS) or (6S,αR) tetrahydrofolic acid, comprising preparing or dissolving an equimolar or a concentrated mixture of a diastereomer of an addition salt of a ~~tetrahydrofolic acid~~ or tetrahydrofolic acid ester with an aromatic sulphonic acid in an organic solvent, wherein the tetrahydrofolic acid or tetrahydrofolic acid ester is of the formula III,



wherein ~~R₁ and R₂ are H, and~~ one of R₁ and R₂ is H and the other represents, or both R₁ and R₂, independently of one another[[,]] represent, a monovalent hydrocarbon radical or a heterohydrocarbon radical attached via a C atom, wherein the heteroatom is -O-, -S-, or -N-,

HA stands for the aromatic sulphonic acid,

and x denotes an integer or a fractional number of 0.5-2.0,

then crystallizing at least once, and optionally hydrolyzing the crystallizate to produce (6S,αS) or (6S,αR) tetrahydrofolic acid, crystallizing the latter as a free acid or isolating the tetrahydrofolic acid in the form of a salt.